

Research**Profile and characteristic of laryngeal cancer in Radiotherapy Department of Hasan Sadikin General Hospital****Afifah Pinakaratna***, **Marhendra Satria Utama****, **Agung Dinasti Permana*****

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ABSTRACT

Background: A laryngeal cancer is often diagnosed in the advanced stage, as the screening has scarcely been conducted. Studies on laryngeal cancer relating to radiotherapy management are hard to find, especially in Indonesia. **Purpose:** To describe laryngeal cancer patients' profiles who received radiotherapy treatment in the period of 2018 to 2019. **Method:** A descriptive quantitative research with a cross-sectional method, conducted at Radiotherapy Department, Hasan Sadikin General Hospital, Bandung. **Result:** From patients' medical record 38 patients with laryngeal cancer were found. Most of the patients were male (86.8%), ranging from age 51-60 (55.3%), occupation office employees (21.1%) and sellers (21.1%), and had a smoking history (52%). The chief complaint was often in the form of hoarseness (76.3%), the location of the cancer was unspecified (31.6%), most of the cells were squamous cell carcinoma (86.8%), and majority was in stage IV (60.5%). Surgery plus radiotherapy was the most common management (50%), and surgery that generally implemented was total laryngectomy (36.8%). Numerous patients also had a pre-surgery tracheostomy (36.8%). Radiotherapy was more often for adjuvant purposes (52.6%). **Conclusion:** Laryngeal cancer is still uncommon, but awareness and screening should be enhanced to prevent late disease findings.

Keywords: hoarseness, smoking, total laryngectomy, tracheostomy**ABSTRAK**

Latar belakang: Kanker laring sering didiagnosis dalam keadaan stadium lanjut, sedangkan skrining pada penyakit ini masih jarang dilakukan. Penelitian mengenai kanker laring yang diterapi dengan radioterapi juga masih sangat terbatas, terutama di Indonesia. **Tujuan:** Untuk menggambarkan profil pasien kanker laring yang menerima radioterapi pada tahun 2018-2019. **Metode:** Penelitian deskriptif kuantitatif dengan metode potong lintang dari rekam medis, yang dilakukan di Departemen Radioterapi Rumah Sakit Hasan Sadikin, Bandung. **Hasil:** Ditemukan 38 pasien kanker laring dari rekam medis. Didapatkan kebanyakan pasien adalah laki-laki (86,8%), rentang usia 51-60 tahun (55,3%), pekerja kantor (21,1%), dan pedagang (21,1%), serta memiliki riwayat merokok (52%). Keluhan utama terbanyak adalah suara serak (76,3%), lokasi kanker tidak spesifik (31,6%), jenis sel terbanyak adalah karsinoma sel skuamosa (86,8%), dengan mayoritas stadium IV (60,5%). Terapi yang paling sering diberikan adalah operasi dengan radioterapi (50%), jenis operasi yang sering dilakukan adalah laringektomi total (36,8%). Trakeostomi juga dilakukan pada beberapa pasien sebelum dilakukan tindakan (36,8%). Radioterapi sering diberikan sebagai terapi ajuvan (52,6%). **Kesimpulan:** Kanker laring tidak umum terjadi, namun karena sering ditemukan dalam keadaan stadium lanjut, maka dibutuhkan peningkatan kewaspadaan dan skrining kanker laring, untuk mencegah terjadinya stadium lanjut.

Kata kunci: suara serak, merokok, laringektomi total, trakeostomi

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INTRODUCTION

Laryngeal cancer is an abnormal growth of cells in the larynx. Globally, the incidence and prevalence of laryngeal cancer have increased by 12% and 23.8%.¹ According to the World Cancer Report 2020, 60% of laryngeal cancer cases occurred in people with low to moderate income, and 50% of cases arise in Asia. In 2018, there were 177,000 new cases and 95,000 mortality cases of laryngeal cancer globally.² Some previous studies mentioned that laryngeal cancer more often appears in males aged 51-60 years old.^{1,3-5} Other risk factors such as alcohol consumption, smoking, occupation, and geography can also influence the development of this cancer.^{4,6,7}

Sex is related to hormone receptor, while lifestyle and occupation are related to organ abuse. Cigarettes contain >70 carcinogens and could influence the alterations of some functions in a cell, such as inflammatory markers and DNA methylation.² Nicotine on cigarettes can increase cells proliferation into malignancy, their survival, and inhibit antitumor in immune response.⁸ Metabolite form of ethanol in alcohol can inhibit DNA methylation and increase the production of reactive oxygen species, leading to cancer. Exposure to some chemical agents/occupational carcinogens, as asbestos and benzene, can also lead to cancer development.²

Symptoms that appear depend on the location of cancer in the larynx. In general, signs and symptoms that emerge as long-lasting hoarseness, coughing, and shortness of breath, need to be suspected as laryngeal cancer. Laryngeal cancer is often detected in the advanced stage, and the results of histopathology findings are often squamous cell carcinoma (SCC).^{9,10} With the increasing

of cancer stage, the survival rate will decrease as low as 40%.¹¹ Although the examination uses more advanced procedures, laryngeal cancers are still often being diagnosed at an advanced stage.¹⁰ Thus, we should understand more about the risk factors, signs, and laryngeal cancer symptoms for early diagnosis. The management of laryngeal cancer could be surgery, radiotherapy, or chemotherapy. For the patient's quality of life in the future, it is necessary to carefully select the therapy procedures. Some factors to be considered while determining surgical and non-surgical procedures are patient's age, comorbidities, the extension of cancers, the function of larynx pre-management, also the availability of expertise and tool-modalities. For early-stage, single modality like transoral laser microsurgery, open partial laryngectomy, or radiation could be an option. Multimodality procedures like chemoradiation are used in advanced stages, while surgery like total laryngectomy that does not consider organ preservation could be used for an advanced stage with poor laryngeal function or contraindication for chemoradiation.¹¹ Extremely advanced conditions as T4b laryngeal cancer or extension to nasopharynx could be very challenging for surgery, or related to poor prognosis, and might need some other options for treatment.¹² Radiotherapy is considered to have a high organ-preservation function in the early stage, and it is combined with chemotherapy in the advanced stage.^{11,13} The quality of life of patients with advanced-stage after radiotherapy treatment is usually good, with limited adverse effect in some cases.¹⁴

Meanwhile, research on the study of laryngeal cancer patients' profiles with radiotherapy procedure is still quite challenging, especially in Indonesia. So, in

this research, the authors wanted to learn more about laryngeal cancer patients that had undergone radiotherapy.

METHODS

This was a descriptive quantitative study using cross-sectional method by tracing patients' medical records in Radiation Oncology Department/Radiotherapy Department, Hasan Sadikin General Hospital, Bandung. This research had received an ethical exemption from the Health Research Ethics Committee of the Faculty of Medicine, Universitas Padjadjaran by number 843/UN6.KEP/EC/2020 and Hasan Sadikin General Hospital number LB.02.01/X.2.2.1/21863/2020.

Research was carried out in September 2020 at the Radiation Oncology Department/Radiotherapy Department, Hasan Sadikin General Hospital, Bandung, using Hospital Based Cancer Registry (HBCR). The population was the whole medical records of patients with laryngeal cancer, who had undergone radiotherapy, from January 1th 2018, to December 31th 2019, that fulfilled

the inclusion criteria. The exclusion criteria were incomplete medical history, or missing medical record, or inaccessible data.

The data were assessed for the profile and the characteristics of clinical laryngeal cancer patients. It included gender, age, occupation, history of smoking and alcohol consumption, and chief complaint. It also covered basic diagnosis, cancer location, type of cell, cancer stage, metastasis, the therapy, and information regarding radiotherapy performed on the patient. Data was collected via Google formula, then processed using Microsoft Excel 2019 and IBM SPSS ver.25.

RESULT

This study results came from medical records of 38 laryngeal cancer patients (2.73%) out of a total of 1,388 patients treated in the Radiation Oncology Department/Radiotherapy Department Dr. Hasan Sadikin, Bandung in the period of 2018-2019. Table 1 showed the frequency distribution of profiles and clinical characteristics of laryngeal cancer patients.

Table 1. Distribution of profiles of laryngeal cancer patients

Characteristics	N=38	%
Gender		
Male	33	86.8
Women	5	13.2
Age		
21-30 years	1	2.6
31-40 years	0	0
41-50 years	8	21.1
51-60 years	21	55.3
61-70 years	8	21.1
>70 years	0	0
Occupation		
Office employees/workers	8	21.1
Farmers	3	7.9
Factory workers	7	18.4
Soldiers/policemen	4	10.5

Housewife	1	2.6
Medical personnel	1	2.6
Teacher	1	2.6
Sellers	8	21.1
Others	4	10.5
Unknown	1	2.6
History of smoking & alcohol consumption		
Both	1	3
Smoking	20	52
Alcohol	0	0
Neither	17	45
Chief Complaint		
Hoarseness	29	76.3
Lump in the neck	3	7.9
Dysphagia	2	5.3
Headache	1	2.6
Bleeding	1	2.6
Post-surgery	1	2.6
Unknown	1	2.6
Basic of diagnosis		
Primary tumor histology	38	100
Cancer location		
32.0 Glottic	5	13.2
32.1 Supraglottic	7	18.4
32.2 Subglottic	2	5.3
32.3 Laryngeal cartilage	1	2.6
32.8 Transglottic	11	28.9
32.9 Unspecified	12	31.6
Type of sell		
Squamous cell carcinoma	33	87
Keratinizing squamous cell carcinoma	1	2.6
Non-keratinizing squamous cell carcinoma	1	2.6
Small cell neuroendocrine carcinoma	1	2.6
Squamous cell papilloma	1	2.6
Chondrosarcoma	1	2.6
Clinical Stage		
I	3	7.9
II	2	5.3
III	10	26.3
IV	23	60.5
Metastasis		
Lung/pleura	1	2.6
Bone	1	2.6
No metastasis	36	94.8

Management		
RT	10	26.3
Surgery+RT	19	50
RT+chemotherapy	7	18.4
Surgery+RT+chemotherapy	2	5.3
Type of surgery		
Total laryngectomy	14	36.8
Laryngectomy with thyroidectomy	2	5.3
Laryngectomy with lobectomy	1	2.6
Laryngectomy	1	2.6
Unknown	3	7.9
No surgery	17	45
Pre-management tracheostomy		
Yes	14	36.8
No	24	73.2
RT indications		
Curative	17	44.7
Adjuvant	20	52.6
Palliative	1	2.6

RT = Radiotherapy

Based on age ranges, laryngeal cancer sufferers were within of 51-60 years (55.3%, n=21), with an average age of 54.89. The youngest patient was 22 years old, and the oldest was 69 years old. Occupation was listed in medical records. Other jobs were entertainer, driver, and retiree. Many patients had history of smoking (52%, n=20). In average, patients smoked as many as 1-2 packs/day.

Patients showed some sign and symptom of hoarseness (76.3%, n=29), lump in neck (7.9%, n=3), dysphagia (5.3%, n=2), headache (2.6%, n=1), and bleeding (2.6%, n=1). However, there were some overlapping symptoms, such as headache with bleeding, or dysphagia with hoarseness. Location and type of cell were based on the International Classification of Disease for Oncology (ICD-O) 3rd edition. Clinical stage was divided based on American Joint on Committee Cancer (AJCC) 8th edition as stage I (7.9%, n=3), stage II (5.3%, n=2), stage III (26.3%, n=10), and stage IV (60.5%, n=23). Stage IV

consisted of IVA (34.8%, n=8), IVB (17.4%, n=4), and IVC (8.7%, n=2).

Management for laryngeal cancer was quite diverse, such as radiotherapy (26.3%, n=10), surgery and radiotherapy (50%, n=19), chemoradiation (18.4%, n=7), and surgery and chemoradiation (5.3%, n=2). There are several types of surgery performed on laryngeal cancer. Three patients underwent total laryngectomy accompanied by radical and modified neck dissection, lateral neck dissection, and selective bilateral neck dissection.

Table 2 was the cross-tabulation of the cancer stadium with some other variables. It showed that advanced-stage was more common in old age, treated with multi-modalities, and underwent tracheostomy before the actual management. It also showed that radiotherapy was indicated as curative for an early stage of cancer, while for advanced stage the radiotherapy was indicated as adjuvant.

Table 2. Stadium with age, management, tracheostomy, indication of radiotherapy

Variables	Stadium (n)				Total
	I	II	III	IV	
Age					
21-30	0	0	0	1	1
31-40	0	0	0	0	0
41-50	2	0	0	6	8
51-60	0	1	8	12	21
61-70	1	1	2	4	8
Total	3	2	10	23	38
Management					
RT	3	2	1	4	10
Surgery+RT	0	0	9	10	19
RT+chemotherapy	0	0	0	7	7
Surgery+RT+chemotherapy	0	0	0	2	2
Total	3	2	10	23	38
Pre-management tracheostomy					
Yes	0	0	2	12	14
No	3	2	8	11	24
Total	3	2	10	23	38
RT indication					
Curative	3	2	1	11	17
Adjuvant	0	0	9	11	20
Palliative	0	0	0	1	1
Total	3	2	10	23	38

RT = Radiotherapy

DISCUSSION

Laryngeal cancer patients at the Radiation Oncology Department/Radiotherapy Department were dominated by male gender (Table 1). These results were similar to those mentioned in earlier studies that laryngeal cancer are more commonly occurs in males.^{1,3,5} A study stated a relationship between hormone receptors and the development of laryngeal cancer, which suggested why this cancer occurs more frequently in men.¹⁵ There are hormone receptors in the vocal fold, relating to androgen, oestrogen, and progesterone.¹⁶ It is also mentioned that presbyphonia in male and female is different because of the effect of these hormones.¹⁷

In this research, in a range of age, laryngeal cancer patients were mostly in 51-60 years of age (Table 1). These results were similar with studies in India.^{3,4} However, Nocini et al.¹ reported different findings, that the incidence had a peak at the age of 65 years, and then a plateau. This result could happen due to the decrease in the ability to repair DNA in connection with increasing age, generating in mutation accumulation. It could also occur in the immune system, causing a declining immune system's ability to fight cancer cells.¹⁸ Also, the shifting of demographics age living over many in the elderly, the resulting burden of cancer can be increased in developing countries.¹⁹

The most common occupation of laryngeal cancer patients were office employees/workers, sellers, and followed by factory workers, there was also one patient having a job as an entertainer (Table 1). According to Fasunla et al.⁹, in Nigeria, the highest number of patients were craftsmen, followed by sellers, retirees, office workers, drivers, teachers, clergymen, farmers, and policemen. In South Korea, the incidence of cancer in some occupations showed the presence of lifestyle socioeconomic inequalities.⁶ High consumption of cigarettes and tobacco are related to high incomes in the country's economy.²⁰ Furthermore, a job that requires a lot of larynx and vocal cord activities, such as a performer, could produce a vocal problem.²¹ In Indonesia, many street merchants offer their merchandises manually and verbally, often using loud voice. It might be an additional factor for the development of laryngeal problem.

In our study, based on history of cigarette smoking and alcohol consumption, many subjects with laryngeal cancer had a smoking history (Table 1). This result was different with Singh et al.³, where the history of alcohol consumption and smoking were the most common. However, the results of this study were similar with those mentioned by Alam et al.⁴ in western Uttar Pradesh. Indonesia is one of the countries with high population of smokers, where the province of West Java has the highest smoking rate in Indonesia (32.7%).^{20,22} Meanwhile, the consumption of alcohol rate in Indonesia is relatively low, only 3%.²² Cancer could suddenly emerge, even though people are not exposed to the risk factors.¹⁸ It was also mentioned that the incidence of laryngeal cancer in male passive smokers was as high as 69.61%.²³ As mentioned above, cigarettes and alcohol contain carcinogenic substances, like nicotine and ethanol, that can induce some alteration in metabolism and lead to cancer development,² so that increasing public awareness about

tobacco and alcohol consumption could help decrease the incidence of laryngeal cancer.²⁴

In our study, the most frequent chief complaint uttered by laryngeal cancer patients was hoarseness (Table 1). This result was the same as what was found by Fasunla et al.⁹ in their study. Because there is a vocal cord in the larynx, its function might be disrupted if cancer spreads into the vocal cord. In our study, reviewed according to the specific location of cancer, laryngeal cancer is mainly located in the supraglottic. This result was same as in India, where the supraglottic was the most common site (80%) followed by the glottic (20%); none of the patients had primary in subglottic.³ Our finding was dissimilar with a study in Nigeria, where there are more laryngeal cancer patients with transglottic sites.⁹ In our study, the most common type of cells found was squamous cell carcinoma (Table 1), and this result was similar with previous researches.⁹

This study found that many laryngeal cancer patients came in advanced-stages, particularly stage IV (Table 1). These results were the same as previous studies, stating that >90% of patients with laryngeal cancer were found in advanced-stages.⁹ Abrahão et al.¹⁰ mentioned that even with the high level of diagnostic procedures, patients were still diagnosed at an advanced stage. The symptoms are frequently unspecific and vague, so it is often disregarded by the patients, and resulting in the development and distant spreading of the cancer.¹ Insurance also considered has a role in the development of the disease, as it was found that patients who did not have insurance had a strong relationship with advanced-stage.⁵

The management that commonly given were surgery and radiotherapy (Table 1). Based on Table 2, the patients with early-stage got radiotherapy, while patients with advanced-stage underwent radiotherapy or multimodalities treatment as their management. Selection of procedures for

treating laryngeal cancer are essential because the purpose is to eradicate the cancer and preservation of the laryngeal function to maximize the quality of life. The factors that need to be considered in the selection of management are size and stage of T, lymph nodes metastasis, physiology function of the larynx, the patient's physical condition and comorbidity, the patient's wish and compliance, and availability of the expert and equipment tools.^{11,25}

Carefully selected patients with favourable early stage of laryngeal cancer should be considered for a single modality of therapy when the possibilities for curing are vast. Single modality options include transoral laser microsurgery, open partial laryngectomy, or radiation therapy alone. In cancer cases with bulky, or deeply invasive T2, total laryngectomy is the only option. Meanwhile, if the physiology of the larynx is still good, functional outcomes will be severely compromised after surgery, and lack of skilled surgeon can be the reason for patients in early-stage are treated radiotherapy.¹¹

Whereas, for laryngeal cancer with locally advanced-stage, organ-preservation surgery, chemoradiation, or radiotherapy alone could become an option, because of the potential to maintain the laryngeal function. For patients with a low laryngeal function/extensive advanced-stage, total laryngectomy can provide higher survival rates and better quality of life.²⁴ This research found that some patients with advanced-stage were not managed with surgery because they were not eligible for this management (Table 2). Either that the cancer had spread to the upper gastrointestinal tract or the mass was fixated, and had a poor surgical prognosis.^{12,24}

In patients who underwent surgery, the most common type of surgery was total laryngectomy (TL) (Table 1). TL is the most common surgical procedure performed on >50% of laryngeal cancer patients in Nigeria.⁹ It is considered the standard treatment

for advanced laryngeal cancer and not recommended for organ preservation due to the spread of cancer to thyroid cartilage and poor laryngeal function.¹¹ Fu et al.²⁵ mentioned that this procedure had an advantage in survival and locoregional control in stage IV laryngeal cancer, but needed more evidence to show that TL was superior to other non-surgical treatments. Quality of life of patients were good in general, but speech function was still the problem.²⁶

This study found that some patients had undergone tracheostomy before curative management (Table 1). According to the cancer stage, the patients who underwent tracheostomy procedure were in advanced-stages (Table 2). Alabi et al.²⁷ stated that laryngeal cancer accompanied by the upper airway obstruction was the second most frequent indication for tracheostomy. However, other research found that tracheostomy in advanced-stage had a decreasing survival rate in general.²⁸ Thus, we need more information about performing tracheostomy in advanced laryngeal cancer cases.

Indications for giving radiotherapy were based on the patient's condition assessment. This study found that radiotherapy was often used as adjuvant therapy (Table 1). In early stages laryngeal cancer, the indication of radiotherapy was curative, while for advanced laryngeal cancer, the indication could be curative, adjuvant, or palliative (Table 2). This result was similar with Tamaki et al.²⁹ that radiotherapy could be curative in early stages cancer. Radiotherapy is also considered to have the advantage of organ preservation in the early stage.¹¹

In advanced stages, radiotherapy could be given as pre-surgery or post-surgery adjuvant therapy, based on histological findings, or T3/T4 supraglottic tumors, N2/N3 lymph nodes, extra nodal expansion, etcetera.¹² Radiotherapy could also be given as palliative therapy for inoperable patients.²⁹

The result of this study could be used as the source of data for further research. Some questions could be raised from this research, such as why that area became the most common area with laryngeal cancer, how insurance influences the development stage of laryngeal cancer, and what were the indications of tracheostomy on laryngeal cancer patients in Hasan Sadikin General Hospital. Limitations of this study were lack of samples, less complete information on some medical records, and human errors. The clinician in charge did not write down the patient's full address, there was no final description of the patient's condition, and did not record whether the patient was using insurance. Meanwhile, there were some factors that might influence the development of cancer or the success of treatment.

Laryngeal cancer is still uncommon in Indonesia, especially in Hasan Sadikin General Hospital, Bandung, representing West Java. Some factors could influence the development of this cancer, such as gender, age, smoking, and occupation. It is necessary to enhance the knowledge and awareness about this issue to decrease the incidence of laryngeal cancer. Management of laryngeal cancer at Radiation Oncology Department/ Radiotherapy Department Hasan Sadikin General Hospital, Bandung, is already in accordance with the standard procedures. It needs further study about the effect of tracheostomy in laryngeal cancer, and other factors that could delay radiotherapy.

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